

**STUDY OF ASSOCIATION BETWEEN SERUM TSH AND THYROID NODULES**

Balaga Venkatarao<sup>1</sup>, Seelam Subramanyam<sup>2</sup>, Srinubabu Kollu<sup>3</sup>, Tutika Narasimha Saikiran<sup>4</sup>, Kolagatla Gayathri<sup>5</sup>

<sup>1</sup>Assistant Professor, Department of General Surgery, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

<sup>2</sup>Associate Professor, Department of General Surgery, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

<sup>3</sup>Senior Resident, Department of General Surgery, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

<sup>4</sup>Postgraduate, Department of General Surgery, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

<sup>5</sup>Postgraduate, Department of General Surgery, Andhra Medical College, Visakhapatnam, Andhra Pradesh.

**ABSTRACT****BACKGROUND**

Thyroid nodules and goitre are common carcinoma occurs in 5% of thyroid nodules. Early detection and treatment is beneficial to prolong the survival. Higher TSH values in patients with thyroid nodule is associated with greater risk of differentiated thyroid carcinoma.

The aim of the study is to-

1. Study the association between serum thyroid stimulating hormone and thyroid nodules.
2. Study the various aetiological factors attributing to the causation of thyroid malignancy.
3. Assess serum TSH concentration as a predictor of thyroid malignancy in patients with thyroid nodules.

**MATERIALS AND METHODS**

This prospective study included 100 patients presenting with thyroid swellings in Department of General Surgery, King George Hospital, Visakhapatnam, during the study period- November 2014 to March 2016.

**RESULTS**

30 patients belonged to age group of 26-35, 28 pts. belonged to 36-45. 82 were women, 18 were men. 32 nodules were more than 4 cms in size. Final HPE showed 17 papillary carcinoma, 2 follicular and 1 medullary carcinoma, remaining were benign. Mean TSH value for colloid goitre 1.84 mIU/lit., adenoma 1.89 mIU/lit., PTC 2.75 mIU/lit., FTC 3.26 mIU/lit., MTC 1.1 mIU/lit.

**CONCLUSION**

Thyroid diseases are common in females. Nodules in male are associated with high chances of malignancy. Swellings that are hard or variable are more likely malignant. Swellings of size 4 or >4 cms are more likely to be malignant. The incidence of malignancy is higher in SNT (36%) compared to multinodular goitre (19%). Mean preoperative TSH value in the present study is  $2.27 \pm 0.80$  mU/L. All patients are euthyroid. The mean TSH value was significantly higher in malignancy than in benign disease, i.e.  $2.72 \pm 1.2$  mU/L vs.  $1.78 \pm 1.40$  mU/L.

**KEYWORDS**

Study, TSH, Thyroid Nodule.

**HOW TO CITE THIS ARTICLE:** Venkatarao B, Subramanyam S, Kollu S, et al. Study of association between serum TSH and thyroid nodules. J. Evid. Based Med. Healthc. 2016; 3(94), 5181-5184. DOI: 10.18410/jebmh/2016/1082

**BACKGROUND**

Thyroid nodule is a common clinical problem. It includes both benign and malignant tumours arising in the thyroid gland. In the India, thyroid cancer accounts for less than 1% of all malignancies (2% of women and 0.5% of men). Thyroid cancers are heterogeneous group of tumours with variable rates of growth, biological aggressiveness, histological responses and response to therapy. Thyroid cancer is responsible for six deaths per 1 million persons annually. Although, thyroid cancer accounts for less than 1%

of all cancers, it is the commonest endocrine tumour that shows a geographic variation in the incidence of tumour type and natural history. Early detection and treatment is beneficial to patient. Clinical parameters raising the suspicion of malignancy, includes male gender, young (<20 years) and old >70 years, large (>4 cms size).

Higher TSH value in patients with thyroid nodule is associated with greater risk of differentiated thyroid carcinoma.<sup>1</sup> As thyroid carcinoma comprises a small percentage of thyroid nodules, doing FNAC in all patients of thyroid nodules may not be a good proposition. So, if there is any biochemical parameter, it has a positive correlation with thyroid carcinoma, it may be a good guide to subsequent FNAC and planning management protocol later.

So, the purpose of this study is to explore the possibility of simple clinical and biochemical criteria like serum TSH levels as a parameter that might predict the likelihood of thyroid malignancy in patients presenting with thyroid nodules with different aetiology.

Financial or Other, Competing Interest: None.

Submission 24-10-2016, Peer Review 30-10-2016,

Acceptance 16-11-2016, Published 24-11-2016.

Corresponding Author:

Dr. Balaga Venkatarao,

#33-4-3, Allipuram,

Visakhapatnam, Andhra Pradesh.

E-mail: balagavenkatarao5115@gmail.com

DOI: 10.18410/jebmh/2016/1082



## AIMS AND OBJECTIVES

- To study the association between serum thyroid stimulating hormone and thyroid nodules.
- To assess serum TSH concentration as a predictor of thyroid malignancy in patients with thyroid nodules.

## MATERIALS AND METHODS

This prospective study included 100 patients presenting with thyroid swellings satisfying the inclusion and exclusion criteria from in-patients registry of Department of General Surgery, King George Hospital, Visakhapatnam, during the study period- November 2014 to March 2016.

### Inclusion Criteria

- Any thyroid swelling.
- Age group above 15 years.
- Thyroid profile especially TSH levels measured before any medical intervention.
- All cases must be clinically and biochemically euthyroid.

### Exclusion Criteria

- Those cases not in euthyroid state.
- Patients in whom serum TSH levels were obtained while on thyroid hormone therapy.
- Secondary malignancies in the thyroid (metastasis).
- Thyroid lymphomas.
- Thyroiditis.
- Grave's disease.
- Patients with comorbid conditions.

All patients were admitted and a detailed history and<sup>2,3</sup> clinical examination was done and investigated as per the written proforma. Informed consent was taken. Thyroid profile and FNAC was done in all cases. All cases that gave consent for surgery were explained about risk and complications of surgery and anaesthesia. Preoperatively, investigations were sent according to protocol. A preoperative indirect laryngoscopy was done in all cases to check for the status of vocal cords. The type of surgery depended on the clinical diagnosis and FNAC report. Correlation of the clinical diagnosis, preoperative TSH levels, cytology and the final histopathological diagnosis was done. Patients were followed up regularly over a minimum period of 6 months.

Statistical analysis has been carried out. Student's t-test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (intergroup analysis) on metric parameters. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

## OBSERVATION AND RESULTS

This was a prospective study done in the Department of General Surgery, King George Hospital, Visakhapatnam. The study period was November 2014 to March 2016. Total number of cases - 100. Total number of confirmed malignancy - 20.

## DEMOGRAPHIC PROFILE

### GENDER DISTRIBUTION OF NODULES

Gender	Number of Patients	Percentage
Male	18	18%
Female	82	82%
<b>Total</b>	<b>100</b>	<b>100</b>

### AGE DISTRIBUTION OF THE STUDY GROUP

Age	Total	Male	Female	Percentage
15-25	15	2	13	15%
26-35	30	5	25	30%
36-45	28	5	23	28%
46-55	14	2	12	14%
56-70	13	4	9	13%

Mean age of thyroid nodules in the study is 39.06±12.03 years. Mean age for malignancy is 44.5 years.

### DISTRIBUTION OF CASES ACCORDING TO THE DURATION OF THE DISEASE

Duration	Number of Patients	Percentage
<1 year	68	68%
1-2 years	18	18%
2-5 years	12	12%
>5 years	02	02%
<b>Total</b>	<b>100</b>	<b>100</b>

Most of the patients in this study were presented with <1 year duration.

### Distribution of the Nodules Based on the Side of Occurrence of the Nodule n=100

Side	Total	Male	Female
Right	42	7	35
Left	23	5	18
Right and Left	35	6	29

Among the 100 patients.

42% patients presented with right-sided swelling.

23% patients with left side.

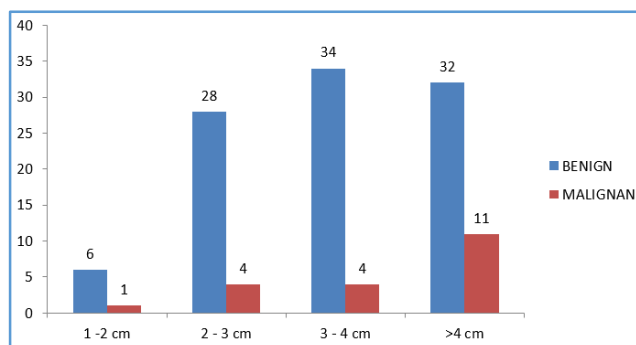
35% presented with right and left-sided swelling.

### DISTRIBUTION OF CASES ACCORDING TO SIZE OF THE NODULE

Size	Number of cases
1-2 cm	8
1-3 cm	24
1-4 cm	35
>4 cm	32

Most of the nodules in this study were more than 3 cm in size.

### Comparison between Benign and Malignancy



Mean size for malignancy =  $3.84 \pm 0.897$ .

Most of the malignant nodules were more than 4 cm in size.

### Histopathology

#### Distribution of Nodules Based on Postop Biopsy in Multinodular Goitre n=35

Biopsy	Total	Male	Female
Adenoma	16	3	13
Colloid	5	14	2
Nodular	7	0	7
Papillary Ca	7	2	5

- Of the 35 cases of multinodular goitre, adenomatous goitre constitute maximum number of cases.
- Papillary carcinoma constitute 7 cases.

#### Distribution of Nodules Based on Postop Biopsy in STN n=65

Biopsy	Total	Male	Female
Adenoma	17	2	15
Nodular	16	2	14
Colloid	19	2	17
Papillary Ca	10	4	6
Follicular Ca	2	2	0
Medullary Ca	1	0	1

### Levels of TSH in Different Types of Carcinomas in this Study

Type	<1 uIU/mL	1-2 uIU/mL	2-3 uIU/mL	3-4 uIU/mL	4-5 uIU/mL	>5 uIU/mL
Papillary	0	5	5	3	4	0
Follicular	0	0	0	2	0	0
Medullary	0	1	0	0	0	0

Differentiated carcinoma like papillary and follicular carcinoma showed higher normal TSH whereas medullary showed TSH value less than 2.

### DISCUSSION

In this study, we had a total of 100 patients who presented with clinically palpable thyroid nodule. The main objective was to evaluate the role of TSH as a biochemical predictor

In the present study, colloid goitre constitutes the predominant variety in STN and papillary carcinoma is the predominant among the malignant nodules.

### Comparison of Different Types of Carcinoma in STN

Type	Total	Male	Female
Papillary	10	4	6
Follicular	2	2	0
Medullary	1	0	1

Papillary carcinoma is the commonest in STN irrespective of the gender.

Type	Total	Male	Female
Papillary	7	2	5
Follicular	0	0	0
Medullary	0	0	0

### Comparison of Different Types of Carcinoma in MNG

Papillary carcinoma is the predominant variety even in MNG

### Average TSH in Different Nodules of Thyroid

Biopsy	TSH (uIU/ml)
Colloid	1.84
Adenoma	1.89
Papillary carcinoma	2.758
Follicular carcinoma	3.26
Medullary carcinoma	1.1

Average TSH in colloid was 1.84 whereas in differentiated carcinomas like papillary and follicular carcinoma was towards higher side of TSH value.

of malignancy. Only patients that were euthyroid were included. Of those patients with confirmed malignancy, a descriptive analysis of the clinical presentation and management done. The observations and results are subjected to statistical analysis and compared with other studies. As thyroid diseases are more common in females, the incidence of thyroid carcinoma is also more in the female sex. Among the 100 patients with thyroid nodule, 20 were

malignant nodules. Among the 20 malignant cases, 12 were females and 8 were males. So, the present study suggests male-to-female incidence ratio in case of carcinoma is 3:2. This signifies male sex is one of the risk factor for malignancy and should be more cautious when a male patient presented with a thyroid nodule. Variation in gender ratio of malignancy maybe due to less number of patients included in the present study than comparative studies. The age distribution of present study is above 15 years. Mean age for thyroid nodule in the present study is  $39.06 \pm 12.03$  years. Mean age for thyroid malignancy is 44.5 years, which is comparable to other studies.<sup>4,5,6</sup> In the present study, incidence of thyroid malignancy is 10% in solitary nodule of thyroid (n=65) and in multinodular goitre (n=35, 7%). Majority of the thyroid nodules in this study group are firm. Majority of the malignant thyroid nodules were variable from firm to hard or hard in consistency. 35% of the thyroid nodules were between 3-4 cm size. 32% of nodules were more than 4 cm in size of which malignant swellings are predominant. In the present study, most common type of malignancy is papillary carcinoma followed by follicular carcinoma.

### POSTOPERATIVE BIOPSY

Adenomatous goitre being the most common. Colloid goitre being the next in benign swellings. In malignancy, papillary carcinoma is the predominant variety followed by follicular carcinoma.

TSH concentrations as a predictor of the diagnosis of malignancy in patients with thyroid nodules. The risk of diagnosis of malignancy rose in parallel with the serum TSH at presentation with significant increases evident in those with TSH  $>0.9$  mIU/l compared with those with lower TSH concentrations.<sup>7</sup> The lowest risk of malignancy was evident in patients with subclinical hyperthyroidism (TSH  $<0.4$  mIU/l) and the prevalence of thyroid cancer was highest in those with subclinical hypothyroidism (TSH  $>5.5$  mIU/l). Haymart et al investigated 843 patients undergoing surgery and recorded the preoperative serum TSH concentration. In this study, the mean preoperative TSH value is  $2.27 \pm 0.80$  mU/L. All patients are euthyroid. The mean TSH value is significantly higher in malignancy than in benign disease, i.e.  $2.72 \pm 1.2$  mU/L vs.  $1.78 \pm 1.40$  mU/L. This is comparable to the results of Haymart et al,<sup>8</sup> Fiore et al.<sup>9</sup>

	Benign	Malignant	P value
Present study	$1.78 \pm 1.40$	$2.72 \pm 1.2$	$P < 0.01$
Haymart et al	$1.4 \pm 0.4$	$3.7 \pm 2.3$	$P < 0.001$
Fiore et al	$0.70 \pm 0.41$	$1.10 \pm 0.6$	$P < 0.0001$

### Comparison average TSH levels in benign and Malignancy

- On comparing mean TSH value of the colloid goitre and the differentiated carcinoma with the t-test, our study has got significant p value of  $<0.01$ .
- This signifies that differentiated carcinomas are TSH dependent and TSH value is more towards the high normal.

### CONCLUSION

Following conclusion have been drawn from the present study:

- Thyroid diseases are common in female population with female-to-male ratio of 4.5:1.
- Mean age for thyroid nodules is  $39.06 \pm 12.03$  years.
- Mean age for malignancy in the present study is 44.5 years.
- Nodules in male are associated with high chances of malignancy.
- Swellings that are hard or variable from hard to firm in consistency are more likely malignant.
- Mean size of malignant nodules in the present study is  $3.84 \pm 0.897$ , so swellings of size 4 or  $>4$  cms are more likely to be malignant.
- Majority of patients presented as solitary nodule. The incidence of malignancy is higher in SNT (36%) compared to multinodular goitre (19%).
- Mean preoperative TSH value in the present study is  $2.27 \pm 0.80$  mU/L. All patients are euthyroid. The mean TSH value was significantly higher in malignancy than in benign disease, i.e.  $2.72 \pm 1.2$  mU/L vs.  $1.78 \pm 1.40$  mU/L.

### REFERENCES

- Pujol P, Daures JP, Nsakala N, et al. Degree of thyrotropin suppression as a prognostic determinant in differentiated thyroid cancer. *Journal of Clinical Endocrinology and Metabolism* 1996;81(12):4318-432.
- Dorairajan N, Pandiarajan R, Yuvaraja S. A descriptive study of papillary thyroid carcinoma in a teaching hospital in Chennai, India. *Asian J Surg* 2002;25(4):300-303.
- History of thyroid and parathyroid surgery. In: Oertli D, Udelsman R. *Surgery of thyroid and parathyroid glands*. Berlin: Springer 2012:1-7.
- Williams NS, Bulstrode CJK, O'Connell PR. Bailey & Love's short practice of surgery. 26<sup>th</sup> edn. CRC Press 2013:747-753.
- Correa P, Chen VW. Endocrine gland cancer. *Cancer* 1995;75(1 Suppl):338-352.
- Jossart GH, Clark OH. Well-differentiated thyroid cancer. *Curr Probl Surg* 1994;31(12):933-1012.
- Boelaert K, Horacek J, Holder RL, et al. Serum thyrotropin concentration as a novel predictor of malignancy in thyroid nodule investigated by fine-needle aspiration. *J Clin Endocrinol Metab* 2006;91(11):4295-4301.
- Haymart MR, Repplinger DJ, Levenson GE, et al. Higher TSH level in thyroid nodule patients is associated with greater risks of differentiated thyroid cancer and advanced tumor stage. *J Clin Endocrinol Metab* 2008;93(3):809-814.
- Fiore E, Rago T, Provenzale MA. Lower levels of TSH is associated to a lower risk of papillary thyroid cancer in patients with thyroid nodular disease: thyroid autonomy may play a protective role. *Endocrine-Related Cancer* 2009;16:1251-1260.